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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,419	10/30/2003	Stacey Patterson	6704-30	7565

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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/697,419	PATTERSON ET AL.	
	Examiner	Art Unit	
	Iqbal H. Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,7-12,14,27 and 31-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7-12,27 and 31-33* is/are rejected.

7)☒ Claim(s) *4 and 14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

In response to a previous Office action, a non-final requirement (mailed on 6/20/2006), Applicants filed a response and amendment received on September 19, 2006. Claims 1-2, 4, 9, 12, 14, 27 and 31-32 are amended. Claims 3, 5-6, 13, 28 and 30 are cancelled. Thus, Claims 1-2, 4, 7-12, 14, 27, and 31-33 are pending in the instant Office action and will be examined herein.

Applicants' amendments and arguments filed on September 19, 2006, have been fully considered but are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Maintained-Claim Rejections - 35 USC § 112 (1st)

Previous rejection of Claims 1-2, 7-12, 27, and 31-33 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has been described in length in previous Office Actions. Applicant's amendments and arguments have been fully considered but are not deemed persuasive for the following reasons.

With respect to the claims 1-2, 7-12, 27, and 31-33 the applicants argue that the entire specification describes codon-optimized nucleotide sequences encoding a bacterial LuxA protein and the specification also describes the claimed invention in more than sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention i.e. Example 2 entitled "Codon-optimized "LuxA and LuxB' beginning on page 5. This example describes, among other things, how to: 1) determine codon-optimized sequences of LuxA and LuxB genes, 2) synthesize the codon-optimized LuxA and LuxB genes, 3) clone these codon-optimized genes into expression vectors, 4) transform bacterial cells with constructs containing these codon-optimized genes, 5) select bacterial clones and sequence the constructs, 6) transfect mammalian cells with these constructs, 7) select mammalian cell clones, 8) perform bioluminescence assays on these mammalian cells, 9) perform in vitro transcription/translation of the codon-optimized genes, and 10) compare expression of the codon-optimized genes vs. wild-type genes in vivo. In addition, an example of a codon-optimized nucleotide sequence encoding a bacterial LuxA protein is presented in the specification as SEQ ID NO: I. Furthermore, for purposes of providing adequate written description it is not required of a specification to disclose (1) examples; (2) actual reduction to practice of the invention; and (3) the known structure of a biological macromolecule. Based on these teachings, a skilled artisan would easily envision a protocol for constructing codon-optimized nucleotide sequences encoding LuxA protein. Therefore, the written description requirement in which a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed. Thus, withdrawal of this rejection is requested.

Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 1-2, 7-12, 27, and 31-33. The examiner acknowledges the amendment to the claims and arguments but disagrees with the applicants' contention that the claimed invention is adequately described. Claims 1-2, 7-12, 27, and 31-33 are directed to a genus of a DNA molecule comprising a codon-optimized nucleotide sequence of any bacterial any LuxA protein.

The genus of any bacterial any LuxA gene encoding polypeptide, required to practice the claimed invention, is a very large genus with the potentiality of being a highly structurally variable genus. Claims 1-2, 12 and 27 still read any bacterial any LuxA gene encoding polypeptide, which is very broad. Many structurally unrelated mutants, variants and recombinants polypeptides are encompassed by the genus recited. Each LuxA gene encoding polypeptide from each bacterial strain would have distinct LuxA protein having different structure and function among each other. In the instant case there is no structural feature, which is representative of all the members of the LuxA recited in the claim. Applicants argue that the specification recites an example of a codon-optimized nucleotide sequence encoding a bacterial LuxA protein, which is presented as SEQ ID NO: I, however claims 1-2, 12 and 27 do not recite anywhere SEQ ID NO: I as bacterial LuxA protein. The specification discloses only a single representative species, which is insufficient to adequately describe the required genus of LuxA encompassed by the claim. Therefore, for the reasons above, the rejection is maintained.

Previous rejection of 1-2, 7-12, 27, and 31-33 under 35 U.S.C. § 112, first paragraph, as failing to comply with enablement requirement, is maintained. This rejection has been described

in length in previous Office Actions. Applicant's amendments and arguments have been fully considered but are not deemed persuasive for the following reasons.

With respect to the claims 1-2, 7-12, 27, and 31-33 the applicants argue that with regard to meeting the enablement requirement of 35 U.S.C. 112, first paragraph, MPEP 2164.08 states that "['a] all that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Applicants also argue "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation". Applicant asserts that because of the high level of skill in the art and the state of the art at the time, the application was filed; one of ordinary skill in the art would not have to perform undue experimentation to make and use the invention as claimed. Applicants' further point to Example 2, page 6 and 16, the specification walks one step by step through the methodology of making codon- optimized nucleotide sequences encoding Lux proteins. In the third paragraph, guidance for determining a nucleotide sequence optimized for expression in mammalian cells is provided. Guidance for identifying where codon substitutions that facilitate increased expression in mammalian cells is then provided, followed by guidance for incorporating the substitutions (e.g., site-specific mutagenesis and PCR). The third paragraph further teaches GenBank accession numbers for each of the wild-type Lux genes into which codon substitutions can be incorporated, and teaches that nucleic acids encoding LuxA, LuxB, LuxC, LuxD, and LuxE derived from other strains or organisms might be used so long as they can be expressed in mammalian cells to generate luminescence.

Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 1-2, 7-12, 27, and 31-33 on enablement issue. The examiner acknowledges the amendment to the claims but disagrees with the applicant's contention that the scope of the claimed invention is adequately described. Claims 1-2, 7-12, 27, and 31-33 are so broad as to encompass any codon-optimized nucleotide sequence encoding any LuxA protein from any bacteria. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of codon-optimized nucleotide sequence encoding any LuxA protein having any codon substitution broadly encompassed by the claims. Many structurally unrelated mutants, variants and recombinants polypeptides are encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one codon-optimized nucleotide sequence encoding LuxA protein.

While as discussed by applicants the specification provides some guidance with regard to how to make and use the codon-optimized LuxA gene, the guidance provided is much too general in nature to enable the full scope of the rejected claims.

Applicants discuss a lot about sequence, structure, and mutation etc; however, none of the claims 1-2, 12 and 27 recite any evidence of such structural feature of the genus. Applicants need

to limit the claim invention by reciting specific genus of bacterial LuxA, what is the source and without specifying the claimed genus, one of ordinary skill in the art would not be able to practice the claim invention, which requires that one of ordinary skill in the art to know or be provided with guidance for making the full scope of bacterial LuxA genes encompassed by the claims. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute **undue** experimentation. The specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification. As previously stated the specification does not establish: the specification does **not** establish: (A) regions of the protein structure which may be modified with higher luciferase activity; (B) the general tolerance of LuxA protein to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any LuxA residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

For all the reasons above, the examiner finds that amendment of claims and applicants arguments does not describe the structural features of claimed genus encompassed by the claims in sufficient detail to overcome the rejection. The structural feature, which is required, is not specified in the claims. Therefore, for the reasons above, the rejection is maintained.

Withdrawn - Claims Rejections- 35 USC § 103

Previous rejection of Claims 1-2, 7-12 and 27-28 under 35 U.S.C. § 103(a) as being obvious over Szittner et al. (J Biol Chem. 1990 Sep 25; 265(27): 16581-7, see IDS), Mao et al.

(Zhonghua Zhong Liu Za Zhi, 2001 Sep; 23(5): 359-62, article in Chinese) in view of Zolotukhin et al. (US Patent 5,874,304, publication 2/23/1999) is withdrawn by virtue of applicants' amendment of claims and arguments.

Previous rejection of Claims 31-32 and 33 under 35 U.S.C. 103(a) as being unpatentable over Szittner et al. (J Biol Chem. 1990 Sep 25; 265(27): 16581-7, see IDS), Mao et al. (Zhonghua Zhong Liu Za Zhi, 2001 Sep; 23(5): 359-62, article in Chinese) in view of Zolotukhin et al. (US Patent 5,874,304, publication 2/23/1999) as applied to claims 1-3, 8-13, 27-28 and 30 above, and further in view of Greer et al. (Luminescence. 2002 Jan-Feb; 17(1): 43-74, Review) and Lowe et al. (US Patent 6,132,983) is withdrawn by virtue of applicants' amendment of claims and arguments.

Summary of Pending Issues

The following is a summary of the issues pending in the instant application:

Claims 1-2, 4, 7-12, 14, 27 and 31-33 are pending.

Claims 1-2, 7-12, 27 and 31-33 stand rejected.

Claims 4 and 14 are objected to as depend on rejected base claim.

Conclusion

Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution. **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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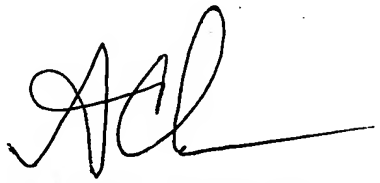

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